

1. A method of making a population of functional hepatocytes for transplantation into a patient, which comprises:

2. The method of claim 1, wherein the hepatocytes are obtained from a human donor.

4. The method of claim 3, wherein the recombinase is Cre recombinase and the recombinase target sites are loxP sites.

5. The method of claim 1, wherein the oncogene is a gene encoding SV40 large T antigen.

6. The method of claim 1, wherein the removable DNA segment further contains a suicide gene, which encodes a gene product that enables destruction of the immortalized
5 cells by an exogenous agent if the removable DNA segment is not removed from the cells.

7. The method of claim 6, wherein the suicide gene is a gene encoding herpes simplex virus thymidine
10 kinase, and the cells are destroyed by exposure to gancyclovir if the removable DNA segment is not removed from the cells.

8. A population of functional hepatocytes
15 produced by the method of claim 1.

9. A method of treating a patient for hepatic failure, comprising transplanting into the patient a sufficient quantity of the hepatocytes of claim 8 to provide
20 hepatic function to the patient.

10. A method of making a population of functional hepatocytes for supporting hepatic function of a patient, which comprises:

- 25 a) providing a sample of primary hepatocytes;
 b) immortalizing the hepatocytes by transforming the hepatocytes with a DNA construct comprising a removable DNA segment containing an oncogene, a selectable marker gene, and a gene encoding herpes simplex virus
30 thymidine kinase, the genes together being flanked on either side by loxP sites;
 c) growing the immortalized hepatocytes; and

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d) reversing the immortalization of the hepatocytes by removing the DNA segment from the immortalized hepatocytes, the removing being accomplished by introducing into the immortalized hepatocytes a gene
5 encoding Cre recombinase to effect excision of the DNA segment at the loxP sites, the excision resulting in the production of the population of functional hepatocytes for supporting hepatic function of a patient.

10 11. The method of claim 10, wherein the hepatocytes are obtained from a human donor.

12. The method of claim 10, wherein the oncogene
15 is a gene encoding SV40 large T antigen.

13. The method of claim 10, wherein the selectable marker gene confers hygromycin resistance to cells expressing the gene.

20 14. A population of functional hepatocytes produced by the method of claim 10.

15. A method of treating a patient for hepatic failure, comprising transplanting into the patient a
25 sufficient quantity of the hepatocytes of claim 14 to provide hepatic function to the patient.

16. An immortalized hepatocyte comprising a primary hepatocyte transformed with a DNA construct
30 comprising two recombinase target sites that flank an oncogene which confers immortalization to the hepatocyte, wherein the immortalization is reversible by excision of the

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oncogene by cleavage at the recombinase target sites when the target sites are exposed to a recombinase that specifically recognizes the target sites.

5 17. The immortalized hepatocyte of claim 16, wherein the recombinase target sites are loxP sites and the immortalization is reversible by Cre recombinase cleavage at the loxP sites.

10 18. The immortalized hepatocyte of claim 16, wherein the DNA construct further comprises a selectable marker gene.

15 19. The immortalized hepatocyte of claim 16, wherein the DNA construct further comprises a suicide gene, which encodes a gene product that enables destruction of the immortalized hepatocyte by an exogenous agent if the oncogene is not removed from the cells.

20 20. The immortalized hepatocyte of claim 19, wherein the suicide gene is a gene encoding herpes simplex virus thymidine kinase, and the exogenous agent is gancyclovir.

25 21. The immortalized hepatocyte of claim 16, wherein the hepatocyte is obtained from a human donor.

30 22. A cell line comprising a population of the immortalized hepatocyte of claim 21, which is cell line NKNT-3.

 23. The immortalized hepatocyte of claim 20,

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wherein the hepatocyte is obtained from a rat donor.

24. A cell line comprising a population of the immortalized hepatocyte of claim 23, which is cell line C8-

5 B.

25. A reverse-immortalized hepatocyte that is functional upon transplantation into a patient, produced by exposing the DNA construct within the immortalized
10 hepatocyte of claim 16 to a recombinase that excises the oncogene by cleavage at the recombinase target sites.

26. A method of treating a patient for hepatic failure, comprising transplanting into the patient a
15 sufficient quantity of the reverse-immortalized hepatocytes of claim 25 to provide hepatic function to the patient.

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